

## Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 1, 36, and 37 have been amended, with claim 37 being re-written in independent form. New claims 92-94 have been introduced, and depend from claim 37. The new claims find descriptive support in original claims 55-57. Therefore, no new matter has been introduced. Claims 1, 36-38, 55-57, and 92-94 remain pending.

Because claim 37 has been re-written in independent form, claims 37, 38, and 92-94 should—at a minimum—be allowable. Applicants otherwise believe all claims as presented are allowable for the reasons asserted below.

The rejection of claims 1, 36-38, and 55-57 under 35 U.S.C. § 112, first paragraph, is respectfully traversed in view of the above amendments and the following comments.

As noted in previous submissions, the specification identifies two species of *dnaN* coding sequences within the claimed subject matter, one from *Streptococcus pyogenes* and the other from *Staphylococcus aureus*, as well as the amino acid sequences of the encoded beta clamp proteins. The specification clearly discloses that *dnaN* encodes a beta clamp useful for highly processive DNA replication. The Examples further support the recited β clamp activity, where it is shown that *Staph. aureus* β interacts with both *Staph. aureus* and *E. coli* (a Gram negative) polymerases on linear DNA (see Example 9 and Figure 5A) but only *Staph. aureus* polymerase on circular DNA (see Example 10 and Figure 5B), and *Strep. pyogenes* β interacts with *Strep. pyogenes* polymerase (see Examples 31, 34, and 35). The sequence data and examples clearly demonstrate that the applicants were in possession of the claimed subject matter.

The PTO has taken the position on page 4 of the office action that applicants must show possession of “coding region of *dnaN* from *all Streptococcus spp.*” (emphasis introduced). Applicants submit that satisfaction of the written description requirement does not require disclosure of all species, but instead merely a representative number.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. See *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) (“[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention

defined by the claims.”). Hence, the PTO must demonstrate *why* the disclosure is insufficient.

The Federal Circuit has clearly espoused that *per se* conclusions of written description violations cannot be founded upon the basis of genus size alone. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1326-27, 63 USPQ2d 1609, 1614-15 (Fed. Cir. 2002) (refusing to adopt position that three species as a matter of law cannot satisfy written description requirement for significantly larger genus). Thus, the PTO’s conclusion cannot be based on genus size alone. But that is precisely what the PTO has done at page 4 of the outstanding office action. Because the PTO’s position is unsupported by law and unsupported by any facts other than genus size, applicants submit that the PTO’s position cannot be sustained.

In addition to the foregoing, the U.S. Patent and Trademark Office (“PTO”) makes several assertions on page 4 that are incorrect and others that appear to be irrelevant to the presently claimed subject matter.

Specifically, the assertion concerning low homology of *delta* subunits is irrelevant to the presently claimed DNA molecules, which encode *beta* subunits.

The assertion that the examples do not demonstrate a function for the *beta* protein encoded by the claimed DNA molecules is incorrect; as noted above, the examples demonstrate that the encoded protein *has* β clamp activity. In other words, a function attributed due to its homology with the *E. coli beta* protein was actually demonstrated.

The assertion that the beta clamp does not assemble onto DNA by itself and requires the assistance of γ complex is not completely accurate. As noted in previous submission and as identified above, the examples demonstrate that γ complex is not required when a replication assay utilizes linear DNA rather than circular DNA.

Because the bases of rejection cited by the PTO are improper, applicants submit that the rejection of claims 1, 36-38, and 55-57 for lack of written descriptive support is improper and should be withdrawn.

The rejection of claims 1, 36-38, and 55-57 under 35 U.S.C. § 112 (1<sup>st</sup> para.) for lack of enablement is respectfully traversed.

The PTO appears to base this rejection on a purported absence of data demonstrating that the claimed *dnaN* DNA molecules (and their encoded beta proteins) are functional in Pol III replication enzymes, confirming that the homology designation of these DNA molecules and subunits is accurate.

As noted above, working examples are provided for two beta subunits, one encoded by *Staph. aureus dnaN* and the other encoded by *Strep. pyogenes dnaN* coding regions. As disclosed in Examples 9–11 (*Staph. aureus*) and Examples 26, 31, and 34–35 (*Strep. pyogenes*), the proteins encoded by *Staph. aureus* and *Strep. pyogenes dnaN* function effectively as beta clamps with Pol III-L (α-large) Gram positive polymerases. Given the **demonstrated ability** of the beta proteins encoded by *Staph. aureus* and *Strep. pyogenes dnaN* to functionally interact with Gram positive polymerases, the two species fully enable the presently claimed invention.

For these reasons, the rejection of claims 1, 36–38, and 55–57 for lack of enablement is improper and should be withdrawn.

The rejection of claim 1 under 35 U.S.C. § 102(e) for anticipation by U.S. Patent No. 6,699,703 to Doucette-Stamm et al. (“Doucette-Stamm”) is respectfully traversed.

Applicants respectfully request reconsideration of the rejection in view of the above amendments and the previously submitted Declaration of Michael E. O’Donnell under 37 CFR § 1.131. Applicants submit that they had invented the presently claimed subject matter prior to July 2, 1997. In particular, applicants had isolated and cloned the *Staph. aureus dnaN* gene, and expressed the encoded beta protein prior to July 2, 1997. Based on the homology between *Staph. aureus* and *Strep. pyogenes*, possession of the *Staph. aureus dnaN* gene is sufficient to establish possession of the presently claimed genus prior to July 2, 1997.

Because Doucette-Stamm is not available prior art under 35 U.S.C. § 102(e), the rejection of claim 1 for anticipation by Doucette-Stamm should be withdrawn.

The rejection of claims 1, 55, and 56 under 35 U.S.C. § 102(e) for anticipation by U.S. Patent No. 6,245,906 to Ueyama et al. (“Ueyama”) is respectfully traversed.

Ueyama, which issued from U.S. Patent Application No. 09/381,862, filed January 11, 2000, is not available prior art. Although the PTO claims the 102(e) date of Ueyama is March 25, 1997, that is improper. As a U.S. patent reference claiming priority from a PCT application filed prior to November 29, 2000, the appropriate 102(e) date is the earlier of the completion of 35 U.S.C. 371 requirements or the filing date of the U.S. application. See MPEP § 706.02(f)(1). Thus, the appropriate 102(e) date is January 11, 2000. This is even stated on the cover page of the reference itself.

Because the present application claims priority to a provisional application filed July 29, 1999, and because the inventors invented the presently claimed subject matter before January 11, 2000 (as evidenced by the previously submitted Declaration of Michael E.

O'Donnell), applicants respectfully request withdrawal of the rejection of claim 1 over Ueyama.

The rejection of claims 1, 36-38, and 55-57 under 35 U.S.C. 112 (second paragraph) is respectfully traversed.

The PTO has asserted that the recitation of "the complement of SEQ ID NO: 27" is unclear. Applicants respectfully disagree. An isolated strand of DNA that contains the *dnaN* coding region, for example, SEQ ID NO: 27, would be expected to hybridize to its complement. The claim language is unclear without such a limitation.

The recitation of "activity as a beta clamp" is not unclear. As described in the background of the invention at page 4, lines 32-33, the beta subunit (encoded by *dnaN*) is a homodimer that forms the ring shaped sliding clamp. This is also known as a beta clamp, as recited in the examples (*see Examples 11, 31, and 34*). Also discussed in the background and in the examples is the interaction between the beta clamp and the polymerase, whereby the beta clamp tethers the polymerase to DNA for processivity. Persons of skill in the art would fully understand what is meant by "activity as a beta clamp."

For these reasons, the rejection of 1, 36-38, and 55-57 under 35 U.S.C. 112 (second paragraph) is improper and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: April 20, 2007

/Edwin V. Merkel/  
Edwin V. Merkel  
Registration No. 40,087

NIXON PEABODY LLP  
Clinton Square, P.O. Box 31051  
Rochester, New York 14603-1051  
Telephone: (585) 263-1128  
Facsimile: (585) 263-1600